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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,403	06/04/2001	Pramod K. Srivastava	8449-178-999	1802

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 11/05/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,403	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,40 and 42-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,40 and 42-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 7/30/2003 (paper no. 15) is acknowledged and entered into the record. Accordingly, claims 2,3,4,37-39, and 41 are cancelled without prejudice or disclaimer and claims 43-49 are newly added.

2. Claims 1,7-9, 40, and 42-49 are therefore pending and examined on the merits.

Information Disclosure Statement

3. The Information Disclosure Statement filed 7/30/2003 (paper no. 14) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections Maintained- 35 USC § 112, 1st paragraph

4. The rejection of claims 1, 7-9, 40, 42 and now newly rejected claims 43-49 under 35 USC 112, 1st paragraph is maintained for the reasons of record. Applicant argues by responding to the 6 points of arguments presented by the examiner. The examiner agrees and concedes to the arguments presented in points 1,2,3 and 4, however, the arguments presented for points 5 and 6 are not considered persuasive.

Point (5): Applicant argues that the specification teaches one of skill how to select an appropriate antigen to complex to the α2M and as such has provided reasonable guidance so as to be enabled for the scope of the invention. This argument is not persuasive because not all antigenic molecules (i.e. epitopes) that display the antigenicity of a tumor specific antigen or infectious diseases agent are useful for the treatment of disease. There are hundreds if not thousands of antigenic molecules that display antigenicity of a tumor specific antigen or infectious disease agent, but knowing the ones that are effective in treatment is critical to the use of the instant invention. The

specification has not provided any guidance to the skilled artisan to determine which one of these hundreds or thousands of antigenic molecules can be used as the antigen and of for that matter which ones when complex to the α2M would be useful for treatment.

Point (6): Applicant argues that the specification teaches antigens that are useful for the "neutralization" of a pathogen infectivity. Furthermore applicant argues that not all embodiments of an invention need be operative for enablement requirements to be satisfied. This argument is not considered persuasive because "neutralization" and prevention are not the same. "Neutralization" is a form of treatment and is not commensurate in scope to preventative products. Many viral diseases such as HIV have to date no know cure or for that matter prophylactic treatment options. Beyrer C (The Hopkins HIV Report 2003 Jan; 15(1):6-7) underscores the importance of establishing a vaccine for preventing HIV, but clearly states that although the parameters for understanding the progression of the disease exist, methods or treatment options are lacking. A reasonable correlation must exist between what is being claimed and that which is disclosed in the specification. The specification has not taught the nexus between "neutralization" and prevention and therefore not enabled for a preventative vaccine. The same holds true for cancer treatment. It is a well known and established fact that cancer in general is an unpredicatable disease of which there is no known cure of prophylactic vaccine. Gura (Science, v278, 1997, pp.1041-1042) discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout

mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. How would the administration of α2M complexed with a tumor specific antigen "prevent" the formation of cancer? The specification has not taught the skilled artisan that such a "vaccine" is available.

Therefore, given the lack of teaching concerning the correlation between treatment and prevention, the specification is not enabled for the full scope of pharmaceutical compositions that comprise α2M complexed to any and all antigenic molecules that displays the antigenicity of a tumors specific antigen or for infections disease agents that are useful for the prevention of a disease.

Claim Rejections Maintained - 35 USC § 102

5. The rejection of claims 1,7-8, and 42 under 35 USC 102(b) as being anticipated by Otto *et al* is maintained for the reasons of record. Applicant argues that the cited reference must teach each and every limitation recited in the claim, wherein the α2M must be complexed to "tumor specific-antigens." Applicant provides two references (see IDS reference EC and ED of paper no. 14) to indicate that PSA is not a tumor specific-antigen because PSA is found on both abnormal and normal prostate tissue. Applicant's arguments have been carefully considered but are not found persuasive. The specification indicates in one of its preferred embodiments of "tumor specific-

antigen" can be a prostate specific antigen (see page 37 lines 18-20). Therefore, the claims as currently amended are still anticipated because Otto *et al* disclose a purified complex of α2M non-covalently associated with PSA, which is, as disclosed by the specification, a tumor specific-antigen.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 7-9, 40, and 42-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth an α2M complexed to a tumor specific antigen or an antigen associated with an infectious disease or agent that is capable of antagonizing an HSP-antigen complex and is therefore not commensurate in scope to an pharmaceutical composition that is capable of treating or preventing a disease comprising an α2M complexed to a antigenic molecule that displays the antigenicity of a tumor specific antigen or an antigenic molecule that displays an antigen associated with an infectious disease or agent.

Claims are drawn to a pharmaceutical composition capable of treating or preventing a tumor/cancer or infectious disease comprising an α2M complexed to either an antigenic molecule that displays the antigenicity of a tumor specific antigen or the antigenicity of an infectious disease or agent.

Although drawn to the DNA arts, the findings of University of California v. Eli Lilly and Co., 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. v. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in the Unviersity of California v. Eli Lilly Co. 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition of the function, as we have previously indicated, does not suffice to define a genus because it is only an indication of what the gene does, rather than what it is Id. At 1568,

43 USPQ2d at 1406. The courts concluded that "naming a type of material generally known to exist, in the absence of knowledge as to that that material consists of, is not description of that material." Id.

Finally the courts addressed the manner by which genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs defined by nucleic acid sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus". Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing it complete structure. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that " the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics … i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between functional and structure, or some combination of such characterisitics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The invention at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. The instant specification may provide adequate written description of the α2M complexed to an antigenic molecule that displays the antigenicity of a tumor specific antigen or an

infectious agent or disease per Lilly, by structurally describing a representative number of antigenic molecules that display antigencity of a tumor specific antigens or an infectious agent by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete " by disclosure of sufficiently detailed relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In the instant case, the specification does not describe the broad genus of antigenic molecules that display the antigenicity of tumor specific antigens or infectious agent required for the practice of the instant invention in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of such antigenic molecules, nor does the specification provide any partial structure of said antigenic molecules, nor any physical or chemical characteristics of the antigenic molecules nor any functional characterisitics coupled with the known or disclosed correlation between structure and function. The recitation of tumor-specific antigen or infectious agent does not limit the structures to those associated with tumor or infectious agents, but rather to any epitope that is found in common to both (i.e. anti-idiotypic antibodies and peptido mimetics that have a common epitope or structure falls within the scope of the antigenic molecules).

The specification describes only tumor antigens and infectious agents. Therefore it necessarily fails to describe a "representative number" of species of any and all

antigenic molecules. In addition, the specification also does not describe "structural freatures common to the members of the genus, which features constitute a substantial portion of the genus."

Thus the specification does not provide an adequate written description of the antigenic molecules to which the claimed α2M can be complex in order for the skilled artisan to practice the instant invention.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
October 27, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
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